DEPARTMENT OF THE AIR FORCE
59TH MEDICAL WING (AETC)
LACKLAND AIR FORCE BASE TEXAS

21 MAR 2016

MEMORANDUM FOR SGVT
ATTN: CAPT LYNDSEY FERRIS

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled **Anoxic Brain Injury Secondary to Metabolic Encephalopathy** presented at **Optometry and Vision Science** with MDWI 41-108, and has been assigned local file #**16110.**

2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.

3. Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are 59 MDW staff member, we can forward your request for funds to the designated wing POC.

4. Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

Linda Steel-Goodwin

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

1. TO: CLINICAL RESEARCH	2. FROM: (Author's Name, Rank, Grade, Office Symbol)	3. GME/GHSE STUDENT:	4. PROTOCOL NUMBER:
	Captain Lyndsey Ferris, SGOO	☐ YES ☒ NO	N/A

5. PROTOCOL TITLE: (**NOTE:** For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.)

Anoxic Brain Injury Secondary to Metabolic Encephalopathy

6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED:

Anoxic Brain Injury Secondary to Metabolic Encephalopathy

7. FUNDING RECEIVED FOR THIS STUDY? ☐ YES ☒ NO FUNDING SOURCE:

8. DO YOU NEED FUNDING SUPPORT FOR PUBLICATION PURPOSES: ☐ YES ☒ NO

9. IS THIS MATERIAL CLASSIFIED? ☐ YES ☒ NO

10. IS THIS MATERIAL SUBJECT TO ANY LEGAL RESTRICTIONS FOR PUBLICATION OR PRESENTATION THROUGH A COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENT (CRADA), MATERIAL TRANSFER AGREEMENT (MTA), INTELLECTUAL PROPERTY RIGHTS AGREEMENT ETC.?
☐ YES ☒ NO **NOTE:** If the answer is YES then attach a copy of the Agreement to the Publications/Presentations Request Form.

11. MATERIAL IS FOR: ☒ DOMESTIC RELEASE ☐ FOREIGN RELEASE
CHECK APPROPRIATE BOX OR BOXES FOR APPROVAL WITH THIS REQUEST. ATTACH COPY OF MATERIAL TO BE PUBLISHED/PRESENTED.

☒ 11a. PUBLICATION/JOURNAL (List intended publication/journal.)
Optometry and Vision Science

☐ 11b. PUBLISHED ABSTRACT (List intended journal.)

☐ 11c. POSTER (To be demonstrated at meeting: name of meeting, city, state, and date of meeting.)

☐ 11d. PLATFORM PRESENTATION (At civilian institutions: name of meeting, state, and date of meting.)

☐ 11e. OTHER (Describe: name of meeting, city, state, and date of meeting.)

12. EXPECTED DATE WHEN YOU WILL NEED THE CRD TO SUBMIT YOUR CLEARED PRESENTATION/PUBLICATION TO DTIC
NOTE: All publications/presentations are required to be placed in the Defense Technical Information Center (DTIC).

DATE	
March 31, 2016	

13. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email)	14. DUTY PHONE/PAGER NUMBER
Ferris, Lyndsey M, Lyndsey.Ferris.2@us.af.mil	210-292-6582

15. AUTHORSHIP AND CO-AUTHOR(S) List in the order they will appear in the manuscript.

LAST NAME, FIRST NAME AND M.I.	GRADE/RANK	SQUADRON/GROUP/OFFICE SYMBOL	INSTITUTION (If not 59 MDW)
a. Primary/Corresponding Author Ferris, Lyndsey M	Capt/O-3	559 THLS/SGOO	
b. Engelke, Carla	N/A	N/A	Southern Arizona VA HCS
c.			
d.			
e.			
f.			

I CERTIFY ANY HUMAN OR ANIMAL RESEARCH RELATED STUDIES WERE APPROVED AND PERFORMED IN STRICT ACCORDANCE WITH 32 CFR 219, AFMAN 40-401_IP, AND 59 MDWI 41-108. I HAVE READ THE FINAL VERSION OF THE ATTACHED MATERIAL AND CERTIFY THAT IT IS AN ACCURATE MANUSCRIPT FOR PUBLICATION AND/OR PRESENTATION.

16. AUTHOR'S PRINTED NAME, RANK, GRADE	17. AUTHOR'S SIGNATURE	18. DATE
Lyndsey M Ferris, Capt, O-3	FERRIS.LYNDSEY.MARIE.1381070391 Digitally signed by FERRIS.LYNDSEY.MARIE.1381070391 Dn: c=US, o=U.S. Government, ou=DoD, ou=PKI, ou=USAF, cn=FERRIS.LYNDSEY.MARIE.1381070391 Date: 2016.02.24 15:01:57 -06'00'	February 24, 2016
19. APPROVING AUTHORITY'S PRINTED NAME, RANK, TITLE	20. APPROVING AUTHORITY'S SIGNATURE	21. DATE
Lt Col Benjamin Franklin	FRANKLIN.BENJAMIN J.10444998 23 Digitally signed by FRANKLIN.BENJAMIN J.10444998 23 Date: 2016.02.24 16:49:39 -06'00'	February 24, 2016

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

1st ENDORSEMENT (59 MDW/SGVU Use Only)

TO: Clinical Research Division 59 MDW/CRD Contact 292-7141 for email instructions.	22. DATE RECEIVED 3/2/2016	23. ASSIGNED PROCESSING REQUEST FILE NUMBER 16110

24. DATE REVIEWED	25. DATE FORWARDED TO 502 ISG/JAC
2 Mar 2016	

26. AUTHOR CONTACTED FOR RECOMMENDED OR NECESSARY CHANGES: ☐ NO ☒ YES If yes, give date. 3 Mar 2016 ☐ N/A

27. COMMENTS ☒ APPROVED ☐ DISAPPROVED

The author added the DoD disclaimer statement to the abstract. Both the abstract and manuscript are approved.

28. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	29. REVIEWER SIGNATURE	30. DATE
Rocky Calcote, PhD, Clinical Research Administrator	CALCOTE.ROCKY.D.1178245844 Digitally signed by CALCOTE.ROCKY.D.1178245844 DN: c=US, o=U.S. Government, ou=DoD, ou=PKI, ou=USAF, cn=CALCOTE.ROCKY.D.1178245844 Date: 2016.03.15 11:31:53 -05'00'	

2nd ENDORSEMENT (502 ISG/JAC Use Only)

31. DATE RECEIVED	32. DATE FORWARDED TO 59 MDW/PA

33. COMMENTS ☐ APPROVED (In compliance with security and policy review directives.) ☐ DISAPPROVED

34. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	35. REVIEWER SIGNATURE	36. DATE

3rd ENDORSEMENT (59 MDW/PA Use Only)

37. DATE RECEIVED	38. DATE FORWARDED TO 59 MDW/SGVU
March 17, 2016	March 18, 2016

39. COMMENTS ☒ APPROVED (In compliance with security and policy review directives.) ☐ DISAPPROVED

Abstract is approved as well.

40. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	41. REVIEWER SIGNATURE	42. DATE
Christopher Carwile, TSgt/E-6, NCOIC, PA	CARWILE.CHRISTOPHER.STEWART.1280477229 Digitally signed by CARWILE.CHRISTOPHER.STEWART.1280477229 DN: c=US, o=U.S. Government, ou=DoD, ou=PKI, ou=USAF, cn=CARWILE.CHRISTOPHER.STEWART.1280477229 Date: 2016.03.16 14:18:55 -05'00'	March 18, 2016

4th ENDORSEMENT (59 MDW/SGVU Use Only)

43. DATE RECEIVED	44. SENIOR AUTHOR NOTIFIED BY PHONE OF APPROVAL OR DISAPPROVAL ☐ YES ☐ NO ☐ COULD NOT BE REACHED ☐ LEFT MESSAGE

45. COMMENTS ☐ APPROVED ☐ DISAPPROVED

46. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	47. REVIEWER SIGNATURE	48. DATE

DEPARTMENT OF THE AIR FORCE
AIR EDUCATION AND TRAINING COMMAND

16 March 2016

MEMORANDUM FOR 59 MDW/CRD

FROM: 502 ISG/JA (Major Mark Coon)

SUBJECT: Ethics Review for Publication Approval Request

1. **BLUF:** A request for a legal review of a journal article titled "Anoxic Brain Injury Secondary to Metabolic Encephalopathy" was submitted by Capt (Dr.) Lyndsey Ferris.
Dr. Ferris plans to publish this piece in *Optometry and Vision Science*, an academic journal. The journal article is legally sufficient as drafted, subject to the guidance provided below.

2. **FACTS:** A journal article titled "Anoxic Brain Injury Secondary to Metabolic Encephalopathy" was submitted for publication. The author plans to publish this research in *Optometry and Vision Science*, an academic journal.

3. **LAWS AND REGULATIONS:** DoD 5500.07-R, Joint Ethics Regulation (JER), section 3-305 establishes the rules governing "Teaching, Speaking and Writing." In accordance with that provision, where a publication will deal in significant part with any ongoing or announced policy, program or operation" of the Air Force, the author is required to include a disclaimer that states that the views presented are those of the author and do not necessarily represent the views of DoD or its Components.

4. **ANALYSIS:** In this case, although the proposed journal article does not "deal in significant part with any ongoing or announced policy, program or operation" of the Air Force, Dr. Ferris' affiliation and/or rank will be included in the article. Moreover, it will be clear that the case study information was obtained as part of her military medical practice. Accordingly, it is prudent for Dr. Ferris to include the abovementioned disclaimer and she has, in fact, done so here. Accordingly, and in light of the fact that there are no other apparent conflicts of interest that would prohibit publication, this journal article is legally sufficient. One should also keep in mind that a Public Affairs review may be needed if one has not already been obtained.

5. **CONCLUSION:** The journal article presented for review contains the legally required disclaimer and is therefore legally sufficient. If you have any questions, please call the undersigned at 671-3362.

MARK E. COON, Major, USAF
Assistant Staff Judge Advocate

I concur.

ARLENE R. CHRISTILLES
Chief, Civil Law

Introduction:

Syndrome of Inappropriate Antidiuretic Hormone (SIADH) is a condition in which the body has normal adrenal cortical function and normal systemic sodium levels, but an "inappropriate" concentration of antidiuretic hormone (ADH) in relation to body fluid osmolality.[1-3] SIADH is a fairly common condition, accounting for up to one-third of all cases of hyponatremia.[1] It can be caused by a variety of conditions, including brain trauma, hormone-producing neoplasms, advanced age (idiopathic), genetics, nervous system or pulmonary disorders, medications, endocrine disease, immunosuppressive disease, and activities such as endurance exercise.[2, 6] Given the wide range of etiologies, SIADH is often broken down into five main categories: malignancy, lung disease, central nervous system disease, drug use, and miscellaneous.[3] Treatment of SIADH is often two-pronged: first, treating the hyponatremic state that is caused by the condition, and second, addressing the underlying etiology of the SIADH.[2, 6-8] Hyponatremia treatment is largely dependent on the severity and duration of onset, but the overarching goal is to increase serum sodium levels without secondary neurological complications. This goal can be achieved through the use of hypertonic saline, loop diuretics with saline, vasopressin-2 receptor antagonist and fluid restriction.[7]

If sudden and severe, hyponatremia can lead to encephalopathy and the development of an acquired brain injury (ABI).[1-3] These injuries can have significant physical, psychological and visual sequelae, which if not managed properly can lead to substantial reductions in quality of life. Proper management involves comprehensive assessment, appropriate therapy tailored to boost the natural neuroplasticity process of the brain, and patient education.

Case Report:

A twenty-four-year-old Active Duty Military Caucasian male reported to the Southern Arizona Veterans Affairs Health Care System's (SAVAHCS) Traumatic Brain Injury (TBI) eye clinic for evaluation and treatment of constant bilateral visual blur, right-sided peripheral vision loss and difficulty reading. The patient denied any medication use. His ocular history was significant for a congenital constant right esotropia, longstanding reduced depth perception, and bilateral overacting inferior oblique muscles. He reported spectacle wear beginning at age five years, but denied any history of previous vision therapy or

treatment for his esotropia. His medical history was significant for a brain injury incurred approximately four months prior during Basic Military Training.

An extensive review of the patient's medical record revealed that eighteen weeks prior he was transported to an emergency room for treatment after being discovered ill in his bunk. Upon presenting to the emergency room, the patient's condition worsened: he became incoherent, suffered a seizure, and developed acute respiratory failure. Diagnostic testing including laboratory work-up, radiology studies, and electroencephalogram (EEG) was performed, and the patient was found to have severe hyponatremia with a serum sodium level of 109 mmol/L (normal 136-145), leukocytosis, with a white blood cell (WBC) count of 26.2 $10^3/mm^3$ (normal 4.3-9.5), and rhabdomyolysis, with a creatine phosphokinase (CPK) value of 3,475 IU/L (normal 39-308 IU/L). Other findings included fever, dysphagia, and an irregular delta wave with generalized slowing on EEG consistent with mild acute encephalopathy.[4] Magnetic resonance imaging (MRI) of the brain showed generalized hyperintensity also consistent with mild encephalopathy. All other diagnostic testing including serum and urine analysis, chest x-rays, and lymphatic vessel density values was normal.

The patient received rapid treatment for his hyponatremia with intravenous (IV) hypertonic saline to increase serum sodium levels. While no evidence of infectious pathogens were detected in either serum or urine samples, the patient was also given IV broad spectrum antibiotics as his elevated WBC count and fever raised suspicion of possible bacterial infection. Given the patient's severely hyponatremic state in the context of his normal extracellular volume (euvolemia) and hormonal levels, he was diagnosed with an acute episode of SIADH with a secondary moderate anoxic brain injury.[1] The patient spent approximately one month hospitalized for his injuries, then spent one week in a non-military inpatient rehabilitation facility for treatment of mild aphasia, ataxia, and right hemiparesis.

Two months after the initial incident, the patient transferred his care to the SAVAHCS, where he was enrolled for healthcare and rehabilitative services secondary to his anoxic brain injury. His initial visit was in the SAVAHCS Eye Clinic for a neuro-ophthalmology consult. Evaluation revealed best-corrected visual acuities (VA) of $20/30^{+1}$ OD and OS, saccadic dysfunction, oculomotor (fixation) dysfunction, and a complete right homonymous hemianopia (Figure 1). The neuro-ophthalmologist referred the patient to

the TBI eye clinic for additional evaluation and treatment and ordered a repeat MRI of the brain (Figure 2), which revealed regions of hyperintensity of the left occipital lobe consistent with areas of increased metabolic function after brain damage.[5]

Eighteen weeks after the initial incident, the patient presented to the TBI eye clinic for evaluation where the authors became involved with his care. His detailed chief complaints included mild bilateral visual blur, right-sided vision loss with trouble ambulating, and reading and information processing difficulties. A detailed examination was conducted (Table 2). Relevant findings included best-corrected VA OD 20/32, and OS $20/20^{-2}$, a 2^{Δ} constant right esotropia at distance and near, a right homonymous hemianopia bifurcating fixation and involving 40 degrees of the patient's right visual fields, saccadic dysfunction with 2^{+} overshooting worse in right gaze, and a visual information processing dysfunction of abnormal form constancy with a Test of Visual Perceptual Skills (TVPS, 3rd ed., Academic Therapy Publications, Novato, CA) score of zero (equivalent age < 4 years old). Accommodative function testing was conducted and revealed reduced accommodative amplitudes of 6.50 D OD and 6.75 D OS. Throughout the examination, the provider conversed with the patient covering a wide variety of topics to assess the patient's range and severity of symptoms. The patient's responses, along with the exam findings, were taken into account when developing the visual management plan.

Visual Rehabilitation:

Vision rehabilitation was chosen to manage the patient's visual symptoms with a therapy plan focusing on techniques to improve oculomotor skills and visual exploration. Visual exploration training, reinforced by ongoing occupational therapy, would address his ambulation concerns. Training consisted of a one-hour in-office session every week with an experienced vision therapist and daily at-home supplemental activities (Table 1).

The patient returned for re-evaluation after five weeks of vision therapy. Post-vision therapy results were generally positive (Table 2). He displayed improvement in his saccadic and visual information processing functions in addition to a significant reduction in his visual symptoms. Saccadic testing revealed trace overshooting and his TVPS form constancy score increased from zero to 16 (equivalent age ≥18 years old). Moreover, the patient noted a complete resolution of his reading difficulties and stated that extended

reading sessions had become comfortable and enjoyable again. He also reported an improvement in his reading comprehension and memory. Finally, the patient described improved ambulation and felt as though his hemianopia was not inhibiting his daily activities.

The patient underwent a total of thirty-six weeks of vision therapy. At the final encounter, the patient continued to show a persistent right homonymous hemianopia, but displayed stable saccadic, oculomotor, and visual information processing skills. He denied any return of his initial visual symptoms and expressed pleasure at the improvement in his visual skills. He was instructed to continue his previously prescribed home-based therapy as a maintenance mechanism.

Discussion:

Syndrome of Inappropriate Antidiuretic Hormone

One of the leading causes of hyponatremia, SIADH is a condition in which antidiuretic hormone is produced in excessive levels in relation to the body's normal osmolality.[1-3] SIADH etiology is generally grouped into five main categories: malignancy, lung disease, central nervous system disease, drug use, and miscellaneous.[2,6] It can affect individuals of any age and health level, but is typically seen in individuals of poor health suffering from chronic disease states.[1-3] The amount of antidiuretic hormone (ADH) secreted by the pituitary gland is based primarily on the concentration of extracellular solute ions (mainly sodium) in the body.[2] It acts on the collecting duct of the nephrons causing increased resorption of water.[2] With higher serum ADH concentrations, more water is reabsorbed into the blood stream thereby causing dilution of serum and resulting in hyponatremia. As this process continues and less water is passed through the kidneys, the urine solute concentration increases, leading to urinary hypernatremia.[2]

The clinical diagnosis of SIADH is largely a diagnosis of exclusion.[3, 5] There are multiple conditions that should be ruled out prior to a diagnosis of SIADH including but not limited to: cerebral salt wasting, cardiac failure, hyperglycemia, vomiting, diarrhea, and polydipsia or polyuria.[1] Current key diagnostic guidelines (Table 3) include normal adrenal cortical and thyroid function, normal water body concentration (euvolaemia), hyponatremia <135 mmol/L and effective serum osmolality <275 mOsm/kg, urinary sodium

concentration >40 mOsm/kg and no recent use of diuretics.[1-3] Once these key guidelines are met, SIADH can further be classified into four subtypes (Table 4), depending on specific clinical findings.[2] Regardless of subtype, treatment of hyponatremia resulting from SIADH is largely dependent on severity and symptomology. In the case of this patient, clinical testing and a thorough medical review ruled out any current or historic pathologic or malignant condition as well as drug use. This narrowed the cause of the patient's SIADH down to the miscellaneous category, which includes subcategories of transient SIADH secondary to nausea, pain or stress, hereditary SIADH, exercise associated SIADH, and idiopathic SIADH.[3] The patient had no previous episodes of SIADH, nor did he have any family history of SIADH. Prior to the onset of SIADH, the patient was in the early phases of Basic Military Training with the United States Army. He was in a high stress environment and was undergoing intensive physical activities. In addition, he was required to partake in specific meal and hydration plans. Any of these factors could have triggered the episode of SIADH. While over-hydration was hypothesized as a possible determinant, the exact causation was never pinpointed, leading to a generalized diagnosis of idiopathic SIADH.

Hyponatremia may result in a range of symptoms, depending largely on the chronicity and severity of the condition. Low-level hyponatremia may have symptoms of mild headache, confusion, concentration and memory lapses, as well as stability and gait changes.[1-2] As the severity of hyponatremia increases, symptoms rapidly elevate and can include limb weakness, disorientation, psychosis, seizures, and respiratory arrest.[2] In cases of moderate to severe acute hyponatremia (serum sodium ≤125 mmol/L in ≤48 hours), encephalopathy can occur due to the rapid change in extracellular osmolality. If not treated promptly, this cerebral edema can result in brain herniation, significant brain damage and even death.[2-3] The patient in this case was diagnosed with a moderate to severe case of acute idiopathic SIADH. His severe hyponatremic state resulted in both respiratory arrest and cerebral edema, both of which contributed to the development of his anoxic brain injury.

Acquired brain injury:

Acquired brain injury (ABI) is a non-congenital injury to the brain. For patients to be diagnosed with an ABI, they generally must have one or more of the following causative conditions documented in their medical record: a period of decreased consciousness level, amnesia, skull fracture, neurological and/or

neuropsychological abnormalities, and/or intracranial lesion(s).[8] The two main ABI categories are traumatic (TBI) and non-traumatic.[8] Traumatic brain injuries are fairly common and have a significant burden on the healthcare system. In the United States over 3.5 million people or approximately 1% of the population, suffered a traumatic brain injury in 2009 alone[9-10]. This accounts for $56 billion in long-term health costs annually.[9-10] TBIs result from penetrating or non-penetrating (concussive) forces on the brain and have gained national attention over the past decade in pastimes such as the National Football League (NFL©) and with military activities including Operation ENDURING FREEDOM (OEF), Operation IRAQI FREEDOM (OIF), and Operation NEW DAWN (OND).[11-13] In fact, TBIs have been characterized as the "signature injury" of recent military operations as studies have shown TBIs to be present in up to 9.6% of all OED, OIF, and/or OND veterans, and in 80-93% of veterans who received polytrauma care.[11, 13]

TBIs can be classified as mild, moderate, or severe with mild TBIs being most prevalent (80%).[9] While not as common, non-traumatic brain injuries encompass a wide range of etiologies ranging from anoxia and metabolic disorders to stroke, neoplasm and even medication use.[8] Data on non-traumatic ABIs are not as robust as with TBIs. In 2013, all causes of non-traumatic ABIs were estimated to have an incidence of 917,000 annually in the United States.[14] Of the multiple potential causes of ABIs, cerebral vascular accidents are the most common (85%) followed by tumor (7%) and then aneurysms (3%).[14-15] Anoxic brain injuries are rare, and national data is not available on their prevalence at this time. While overall healthcare costs for non-traumatic brain injuries are not currently available, healthcare costs related to strokes alone is estimated at $34 billion annually.[15] Brain injuries often result in both short and long-term physical, cognitive and psychological symptoms, including visual dysfunction. As such, patient management including proper diagnostic evaluations and therapeutic management is critical to long-term recovery.[8-9, 16]

The sequelae and recovery of ABI largely depend on the location, severity, and chronicity of damage.[8-9, 16] The brain is capable of biochemical, physiological and anatomical recovery and reorganization (i.e. neuroplasticity) at any stage in life.[17-18] The neuroplasticity process is naturally occurring and can be broken down into two main categories or phases: recovery and compensation.[17] The recovery phase

involves affected tissue recovering its initial function.[18] In the compensation phase new tissue takes over a function originally performed by the damaged tissue.[18] These phases are not mutually exclusive and often occur synergistically.

When it comes to rehabilitation or active engagement of the recovery and compensation phases of neuroplasticity, providers should be cognizant of neural strategies for improvement.[16-18] After injury, it is very common for patients to develop avoidance patterns on tasks they now find difficult. Lack of engagement hinders the neuroplasticity process, minimizing the ability of the patient to recover and adapt to their post-ABI state. Therefore, rehabilitation should be aimed at actively engaging the patient, and should involve three basic stages: resuscitation, recruitment, and retraining.[18] Resuscitation means engaging the previously damaged regions of brain tissue, recruitment involves engaging new brain tissue regions; and retraining focuses on training either damaged or normal tissue to perform new tasks.[18] Finally, providers should be aware of the general timeline for ABI recovery. Studies reveal that visual recovery peaks between three and six months post-brian injury in stable disease.[19-22] After six months, it is unlikely that further recovery vis resuscitation will occur. However, the ability of the brain to adapt via recruitment and retraining does not decrease, and can persist indefinitely, given continued patient engagement.[18-20]

The patient in this case began vision therapy while in the peak phase of ABI recovery, and concluded active vision therapy almost nine months after his initial injury. While the patient presented with significant symptomology and oculomotor dysfunction, he had largely been avoiding the activities causing him the greatest ocular discomfort. Active engagement via vision therapy targeted the patient's rehabilitative pathways and resulted in significant improvement of this patient's skills and in the near complete relief of his reported symptoms. At nine months post-injury, it is highly unlikely the patient would experience any additional improvement in his visual system because the neuroplasticity process of resuscitation is likely complete. However, the patient might benefit from continued therapeutic intervention as maintenance mechanisms to strengthen his newly re-developed visual pathways. In fact, throughout his treatment regimen, the patient continued to express his satisfaction with his treatment plan, and when asked, maintained that he felt the therapy was beneficial for him in improving his visual

function. As demonstrated in this case, the ability of providers to recognize the phases of the neuroplasticity process and the typical recovery timeline can enhance rehabilitative outcomes by guiding patient-specific management strategies to maximize the rehabilitative process.[17-18, 21]

Visual dysfunction secondary to ABI can impact every part of the visual system due to the complex afferent and efferent nature of the visual pathway, and the high degree of cognitive interpretation.[8-9, 21-24] Patients often report long-term symptoms across multiple facets of their visual system including oculomotor dysfunction (0-56%), photophobia (0-16%), visual blur (19-66.7%), dry eye (9-10.4%), visual field loss (0-38.8%), diplopia (3-40%), and information processing dysfunction (51-59%).[8-9,25] Due to the prevalence of these symptoms, patients often present to their local eye care provider seeking evaluation and treatment.

Regardless of the nature of the ABI, a comprehensive evaluation of the visual system is critical in identification and quantification of visual sequelae. These sequelae can be broken down into four main categories: ocular motility, visual information processing, accommodation/vergence, and visual field defects (Figure 4). Within these categories, providers should ensure binocular vision testing is conducted to provide quantitative evaluations of visual function. Goodrich et al. developed excellent guidelines for examining patients with TBI as part of their Delphi Study.[26] These guidelines include seven procedures recommended for each TBI evaluation to assess the main oculomotor categories of visual sequelae, but do not include assessments of visual processing.[26] At a minimum, testing should include evaluations of best-corrected visual acuity, extra-ocular movement, cover test, near point of convergence, saccades, pursuits and fixation.[14, 26] Accommodation and vergence assessments should include amplitude and facility. Visual fields should be evaluated utilizing confrontations. If a deficit is suspected, automated visual field testing should be performed. Finally, while not as common in the general optometric repertoire, providers should evaluate the patient's visual information processing system including testing for visual neglect and memory, form constancy, midline shift, automaticity and spatial awareness.[21] By evaluating these regions, providers will be able to determine the type and extent of the patient's visual dysfunction (Table 5) allowing for development of an appropriate management plan.[10, 18, 20, 22]

The patient in this case had ABI-related sequelae involving multiple systems including vision, speech, and fine and gross motor muscle control. His visual system sequelae included oculomotor, visual field, and visual information processing deficits. His fixation and saccadic dysfunction, specifically his saccadic overshooting worse in right gaze, can be attributed to the dense scotoma in his right visual field. The patient could track a moving object (pursuit), but as it moved into his right field scotoma, he lost the object and overshot his fixation, having to track back and re-fixate using his functioning left visual field to locate the object again. In the area of visual-perceptual skills, testing revealed the patient suffered from reduced form constancy, which is the ability of a person to perceive an object and find it among other forms, regardless of size, orientation or color.[27-29] Abnormal form constancy can 1) affect a patient's reading ability -especially with changes in font style, color or size-, 2) impact spatial awareness including size constancy and distances-, and 3) cause problems with attention and focus.[28] In this case, the patient's reduced form constancy at his initial neuro-ophthalmology visit and early TBI eye clinic visits may have contributed to his mild reductions in visual acuity.

As was demonstrated in this case, proper management of visual dysfunction often involves active rehabilitation in the form of vision therapy. Vision therapy is widely used to treat a multitude of visual dysfunctions, and multiple studies have shown its effectiveness for treating disorders of the visual system, especially in ABI patients.[21, 30-32] Thiagarajan et al. noted up to an 80% improvement in the visual status of mild TBI patients after only six weeks of bi-weekly therapy sessions.[30] Therapy should focus on the regions suffering deficits and, if managed properly, it may bolster the natural neuroplasticity process.[17-18, 20, 30] There are a multitude of vision therapy tasks that can be chosen and tailored specifically for the patient's visual dysfunction.[18, 20, 22, 25] The key to maximizing patient recovery is maintaining active patient engagement.[17-18] As such, providers should be aware of the various uses of vision therapy activities and understand that any one particular activity can be modified to target desired visual functions, maintain appropriate challenge levels, and enhance patient interest levels.[18, 20] Modification will also help prevent false positive gains secondary to patient familiarity with a given task. For example, a patient may be presented with a rotator and asked to follow a specific target around as the table rotates; this activity primarily engages the oculomotor (fixation and pursuit) system. As the patient begins to master the task, the provider can make the task more complex by giving the patient pegs to place on the rotating board in

different patterns, requiring the patient to follow specific color schemes or placement strategies while placing those pegs, providing distractions in the form of extraneous noise (e.g., music, requiring the patient to state certain words or carry a conversation) or even requiring the patient to maintain certain postures (e.g., sitting, standing on one leg, balancing on a balance board, etc.) while performing the activity. Any task can be modified and keeping that concept in mind aids providers in developing and adjusting therapeutic management to maximize patient engagement and recovery.[17-18, 20]

In addition to the visual system, providers should also be aware of the psychological and physical sequelae from which ABI patients may be suffering. Studies have shown that intensive therapy targeting the sequelae of ABIs can lead to earlier and more long-term improvement in symptoms. [25, 33] These patients should receive appropriate systemic rehabilitative care as early in their recovery phase as possible.[29] Rehabilitative therapy with active patient engagement is key to maximizing recovery, not only through the visual pathways that eye care providers are so familiar with, but also through other disciplines such as physical and/or occupational therapy.[10, 16-18, 24, 33] Providers should determine if their patients are receiving appropriate systemic care for their ABI, and if not, have a general network of health care providers to which they can refer their patients for additional rehabilitative services. The patient in this case was enrolled in the Veterans Affairs Polytrauma System of Care and received care for the multiple systems impacted by his ABI including visual and occupational therapies. Specialists were able to actively monitor the patient's progress in all facets of therapy and communicate with fellow healthcare providers when necessary. This interdisciplinary approach ensured the patient was receiving appropriate healthcare for his sequelae and helped to bolster the rehabilitative process. Regardless of patients' backgrounds, if providers suspect the presence of acquired brain injury and the patient is not receiving the appropriate systemic care, referral to a primary care doctor and/or general neurologist for an initial assessment is warranted, with the understanding that the patient may be further referred to subspecialties for additional care.

Conclusion:

Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH) is a metabolic condition that causes hyponatremia, and in severe cases, encephalopathy and brain injury. Acquired brain injuries

result from any non-congenital insult to the brain and are fairly common. They can cause significant physical, functional and psychological disturbances. Damage to the visual pathways can produce visual field, ocular motility and binocular deficits. As such, the visual system should undergo a comprehensive evaluation to determine the extent of ocular and visual involvement, and management should be actively tailored to boost the natural neuroplasticity process and challenge the patient's specific areas of dysfunction to achieve their goals. Comprehensive rehabilitative treatment is important and patients should be advised to seek care for their non-visual complications. Finally, some recovery and adaptation can be expected, but it is largely influenced by patient engagement. Proper education on expectations and participation are critical to maximize patient buy-in, enhance the rehabilitative process, and improve the patient's quality of life.

Disclaimer:

The views expressed are those of the authors and do not reflect the official views or policy of the Department of Defense, Department of Veterans Affairs or its Components.

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Figure Legends:

Figure 1: Automated visual field testing conducted 2 months after the initial incident showing a homonymous hemianopic defect.

Figure 2A/B: T_2-weighted fluid attenuated inversion recovery (FLAIR) MRI of the brain (A, axial view) (B, coronal view), conducted 3 months after initial incident; note the regions of hyperintensity on the patient's left occipital lobe.

Figure 3: Common Visual Sequelae of Acquired Brain Injury

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